

Comparative data of experiments for the preparation of 4-[1-(1,2,4-triazolyl)methyl]-benzonitrile as per US Patent 5,473,078 and as per ISLL method:

S. No.	B. No.	Yield	Purity	Isomer	Process used	Remarks
1	RD-2/008	0.40	57.66%	40.48%	as per US 5,473,078 : A solution containing alpha bromo-4-toluonitrile (25.0 g) and 1,2,4-triazole (38.9g) in a mixture of chloroform (312.5 mL) and acetonitrile (62.5 mL) is stirred at reflux for 15 hours. The solution is cooled and washed with 3% aqueous sodium bicarbonate (250 mL) and the organic solution is then dried (Na ₂ SO ₄) and evaporated to get a mixture of 4-[1-(1,2,4-triazolyl)methyl]-benzonitrile and 4-[1-(1,3,4-triazolyl)methyl]-benzonitrile in a ratio of about 50:50	HPLC graph attached as Annexure 1
2	RD-2/009	0.60	96.24%	2.47%	ISLL Method, To a solution of 8.9 g of sodium salt of 1,2,4 triazole in 10 cc of dimethylformamide, a solution of 9.0g of 4-Bromomethyl benzonitrile in 20 cc of dimethylformamide at 15-20° C was added over 10 minutes. After the completion of addition, the reaction mixture was stirred at 10-15° C for further two hours. Sodium chloride solution (60 cc) was added and the reaction mass was extracted with dichloromethane (60 cc). The organic layer was washed with water (2x60 cc) and was distilled off. The crude was crystallized from diisopropyl ether to afford 4-[1-(1,2,4-triazolyl)methyl]-benzonitrile	HPLC graph attached as Annexure 2

3	RD-2/010	0.53	98.23%	1.33%	ISLL Method, To a solution of 44 g of sodium salt of 1,2,4 triazole in 50 cc of dimethylformamide, a solution of 47 g of 4-Bromomethyl benzonitrile in 100 cc of dimethylformamide at 10-15° C was added over 30 minutes. After the completion of addition, the reaction mixture was stirred at 10-15° C for further two hours. Sodium chloride solution (300 cc) was added and the reaction mass was extracted with dichloromethane (300 cc). The organic layer was washed with water (750 cc), and was distilled off. The crude was crystallized from diisopropyl ether to afford 4-[1-(1,2,4-triazolyl)methyl]-benzonitrile	HPLC graph attached as Annexure 3
4	RD-2/011	0.55	97.73%	1.53%	ISLL Method, To a solution of 29.6 g of sodium salt of 1,2,4 triazole in 30 cc of dimethylformamide, a solution of 31 g of 4-Bromomethyl benzonitrile in 75cc of dimethylformamide at 10-15° C was added over 10 minutes. After the completion of addition, the reaction mixture was stirred at 10-15° C for further two hours. Sodium chloride solution (180 cc) was added and the reaction mass was extracted with dichloromethane (180 cc). The organic layer was washed with water (500 cc) and was distilled off. The crude was crystallized from diisopropyl ether to afford 4-[1-(1,2,4-triazolyl)methyl]-benzonitrile.	HPLC graph attached as Annexure 4